## REMARKS

A check for the fees for a three month extension of time and a Notice of Appeal were previously submitted. Any fees that may be due in connection with the filing of this paper or with this application during its pendency may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

Claims 18-22 and 35-41 are pending in this application. Claims 18-22 and 35-41 are allowed. Allowed Claim 39 is rewritten as an independent claim incorporating the limitations of its base claim; and rejected Claims 17, 31 and 33 are cancelled herein, thereby placing the application in condition for allowance. No new matter is added.

Claims 17, 31 and 33 are cancelled herein in the interest of advancing the application to allowance. Applicant reserves the right to file continuation application(s) directed to any cancelled subject matter.

**The Rejection of Claims 17, 31 and 33 under 35 U.S.C. §103**

Claims 17, 31 and 33 are rejected as being unpatentablee udner 35 U.S.C. §103(a) over Nolan *et al.* (WO 00/34436) in view of Neves *et al.* (*Bioconjug. Chem.* (2000) 11:51-55), for reasons of record. The Examiner maintains that Nolan *et al.* teaches "the use of a chromosome that is labeled;" in methods that include a step of labeling the chromosome prior to it's introduction into a cell because Nolan *et al.*, while providing examples only of methods in which the chromosome is labeled after delivery into the cell, "specifically states that variations of their method are contemplated." The Examiner concludes that the teachings of Nolan *et al.*, when combined with Neves *et al.*, which allegedly teaches labeling DNA with a fluorescent label, transfecting the labeled DNA into cells and determining the efficiency of transfection by fluorescence microscopy, leads to the claimed subject matter because replacing the "small" DNA molecule of Neves *et al.* with the "large" DNA molecule recited in the claims is a mere "scaling up" in the size of the molecule used in the procedure.

This rejection is respectfully traversed. Also, it is noted that cancellation of the rejected claims renders this rejection moot. Nevertheless, Applicant respectfully disagrees with the Examiner. A mere statement in Nolan *et al.* that "variations" are contemplated provides no teaching or suggestion as to what the variations with respect to the order of exposure of the cell, the chromosome and the label to each other might be. Further, even assuming specific teachings or suggestions in the general term "variations," Nolan *et al.* does not teach or suggest any method of monitoring the delivery of large nucleic acids into cells as

instantly claimed. Neves *et al.*, directed to the delivery of labelled small (7 kb) plasmids into cells, provides no teaching or suggestion for adapting its method to monitoring the delivery of labeled large (0.5 Mb or greater) nucleic acid molecules, whose size and secondary/tertiary structure pose challenges such as the ability to deliver them efficiently into cells, sufficient accessibility to sites for efficient labeling, low specificity of labeling due to a low label/size ratio, and the disruption of secondary and/or tertiary structure upon labeling. Contrary to the Examiner's assertion, the instantly claimed methods are not merely a "scale-up" of the method of Neves *et al.* because as discussed, large nucleic acids are not merely a linear extension of small nucleic acids. Therefore, Neves *et al.* does not cure the deficiencies of Nolan *et al.* and the two references, singly or in combination, do not render the rejected claims obvious.

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In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

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